REMARKS

Reconsideration of the above-identified application is respectfully requested.

Claims 25, 32 and 34 have been amended. No new matter has been added as a result of these amendments.

Rejection of Claims 25-34 under 35 U.S.C. Section 101

Claims 25-34 are rejected under 35 U.S.C. Section 101 as lacking a credible, substantial, specific or well-established utility.

The claimed invention is directed to certain purified polynucleotides, namely SEQ ID NOS:1-14, recombinant expression systems, a cell transfected with said recombinant expression system and a method of producing a polypeptide having at least one epitope.

In Applicants previous response, evidence was submitted demonstrating the identity between BS203 and a protein known as GERP. In response to this evidence, the Examiner states that the finding that GERP is expressed in adenocarcinomas does not indicate that GERP nucleic acids can be used to diagnose adenocarcinomas or breast cancer. The Examiner then points to an article by Vincent that teaches that GERP is expressed in normal breast cells, as well as in normal brain, lung, placenta, kidney, muscle and germinal center B cells. The Examiner goes on to state that the reference does not teach that there is a difference in the level of expression of GERP in normal breast cells versus adenocarcinoma or breast cancer cells. According to the Examiner, Vincent does not teach that GERP nucleic acids can be used to diagnose adenocarcinomas or breast cancer. Therefore, the Examiner concludes that "...the specification has not established that the expression of the instantly claimed BS203 nucleic acids is correlated with breast cancer and has not adequately enabled one of skill in the art to use the claimed nucleic acids for the diagnosis of breast cancer."

As discussed in Example 1 on pages 52, EST's corresponding to the consensus sequence of BS203 were found in 27.8% (5 of 18) of breast tissue libraries. EST's

corresponding to the consensus sequence of SEQ ID NO:14 (or fragments thereof) were found in **only 3.4%** (12 of 355) of the other non-breast libraries. The consensus sequence or fragment thereof was found more than **22** times more often in breast than in non-breast tissues.

As discussed in the specification beginning on page 3, there is a need in the art for the identification of new markers that can be used in the management of patients suffering from breast disease. More specifically, such markers could be used to monitor for the elevated expression of such markers in inappropriate body compartments (i.e, outside of their normal host tissue, the breast) (See, specification, page 3, lines 17-20). The identification of such expression outside the normal host tissue would indicate breast disease. Examples of other well-known markers that are used in a similar manner are prostate specific antigen (PSA) and carcinoembryonic antigen (CEA). PSA is normally secreted at high levels into the seminal fluid and is present in very low levels in the blood of men with normal prostates. However, in patients with diseases of the prostate, including benign prostatic hyperplasia (BPH) or adenocarcinoma of the prostate, the level of PSA is markedly elevated in the blood and is a strong indication of disease of the prostate.

Similarly, CEA is a normal component of the inner lining of the colon and is present stool and in blood at low levels in people without disease of the colon. However, in disease of the colon, including inflammatory bowel disease and adenocarcinoma of the colon, the concentration of CEA is markedly elevated in the blood plasma or serum of many patients and is an indicator of disease of that tissue (such as colorectal cancer).

Additionally, like BS203, PSA and CEA are expressed in a few tissues other than the colon and prostate. Nonetheless, these markers are still recognized as useful in the diagnosis of disease of their primary tissue of origin due to their strong tissue selectivity.

Tumors (cancers) of unknown origin (also known as cancers of unknown primary site) are unfortunately a huge medical problem. The exact incidence of these tumors/cancers is unknown, because many of these patients are "assigned" other diagnoses and are not represented accurately in tumor registries. (See *Cancer Principles & Practices of Oncology,* Lippincott Williams & Wilkins, page 2537). It is believed that cancers of unknown origin accounted for 2% of all cancer diagnoses reported by Surveillance, Epidemiology and End Results registries between 1973 and 1987. *Id.* Some scientists, however, believe that a more realistic estimate of the incidence of these patients is 6% of all invasive cancers in the United States per year (approximately 80,000 to 90,000 patients). It is important for the clinical physician to identify the origin of such tumors/cancers in order to develop an appropriate treatment regimen for the patient. This is important because over the last few decades, several important oncologic issues have changed. *Id.* Combination chemotherapy, often used with surgery or radiation therapy, have proved to be potentially curative for selected patients with several metastatic tumors. *Id.* In addition, palliation and prolongation of survival have been demonstrated after systemic therapy for patients with many other tumor types. *Id.* Furthermore, treatment continues to evolve and improve. *Id.* Such therapeutic improvements have relevance for patients with tumors/cancers of unknown origin, because some have responsive neoplasms. *Id.* Therefore, there is a need in the art for new markers, such as BS203, that can be used to identify such tumors/cancers of unknown origin.

Moreover, as discussed in the enclosed Declaration of Dr. Paula Friedman submitted in connection with the Amendment and Response mailed on January 11, 2001, BS203 is characteristic of a tissue specific marker and is capable of acting as a cancer diagnostic. Therefore, to one of ordinary skill in the art, the presence of BS203 outside of breast tissue would indicate cancer development of that tissue, just as the presence of CEA and PSA outside of their respective tissues indicates cancer of the colon and prostate, respectively.

35 U.S.C. Section 101 has two purposes. First, 35 U.S.C. Section 101 defines the categories of inventions that are eligible for patent protection. An invention that is not a machine, an article of manufacture, a composition or a process cannot be patented. Second, 35 U.S.C. Section 101 serves to ensure that patents are granted on only those inventions that are "useful". *Manual of Patent Examining Procedure* Section 2107.01 (8th Edition, August 2001). Therefore, to satisfy the requirements of 35 U.S.C. Section 101, an applicant must claim an invention that is statutory subject matter and must show that the claimed invention is "useful" for some purpose, either explicitly or implicitly. *Id.*

To be "useful" for some purpose, the invention must have a specific and substantial utility (i.e. "a practical utility"). A "specific" utility is specific to the subject matter claimed (versus a "general utility" that would be applicable to a broad class of invention). A "substantial utility" defines a "real world" use. Not only must the invention have a specific and substantial utility, but this utility must be credible. Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (e.g. test data, affidavits or declarations from experts in the art, patents or printed publications). *Manual of Patent Examining Procedure* Section 2107 (8th Edition, August 2001). An applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement. *Id.*

To properly reject a claimed invention under 35 U.S.C. Section 101, the Examiner must (a) make a *prima facie* showing that the claimed invention lacks utility, and (b) provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing (*Manual of Patent Examining Procedure* Section 2107.02 (8th Edition, August 2001)). The Examiner must do more than question the operability of the invention. Specifically, the Examiner must set forth factual reasons that would lead one skilled in the art to question the objective truth of the statement of operability. *Id.*

In view of the above arguments and the evidence presented in previous Amendments, Applicants respectfully submit that the Examiner has failed to make a *prima facie* showing that the claimed invention lacks utility. However, even assuming *arguendo* that the Examiner has made a *prima facie* showing that the claimed invention lacks utility, the Examiner has failed to provide a sufficient evidentiary basis for her factual assumptions relied upon in making this showing. Specifically, the Examiner has not provided any evidence refuting or contracting the statements supporting utility made in the Declaration of Dr. Friedman. Clearly, Dr. Friedman is one of ordinary skill in this art.

Therefore, Applicants submit that the rejection of claims 25-34 under 35 U.S.C. Section 101 is improper and should be withdrawn.

Rejection of claims 25-34 Under 35 U.S.C. Section 112, First Paragraph

Claims 25-34 are rejected under 35 U.S.C. Section 112, first paragraph as not being supported by a specific or substantial or credible asserted utility or a well-established utility. Applicants respectfully traverse this rejection.

Applicants herein incorporate by reference their arguments made above in connection with the 35 U.S.C. Section 101 rejection. Therefore, in view of said arguments, Applicants submit that this rejection is improper and should be withdrawn.

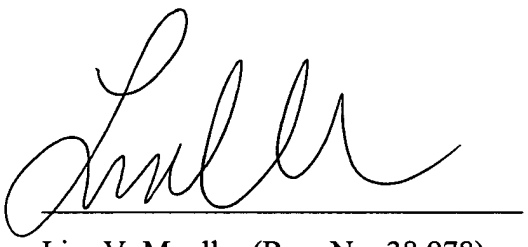
Rejection of Claims 25 and 28-34 Under 35 U.S.C. Section 112, First Paragraph

Claims 25 and 28-34 are rejected under 35 U.S.C. Section 112, first paragraph as not being adequate described by the specification. Claims 25, 32 and 34 have been amended to remove the "comprising" from the claims. This transition word has been replaced with the transition word "consisting of". In view of these amendments to the claims, Applicants submit that this rejection is now moot and should be withdrawn.

Applicants submit that the claims are now in condition for allowance.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge Deposit Account No. 23-0785.

Respectfully submitted,



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